UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,358	11/19/2003	Swen Holder	02481.1834	3767

22852 7590 02/28/2007

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
HABTE, KAHSAY	
ART UNIT	**PAPER NUMBER**
1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/715,358	HOLDER ET AL.	
	Examiner	Art Unit	
	Kahsay Habte	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-24,26 and 31-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *8,24,31 and 33* is/are allowed.

6)☒ Claim(s) *9-23, 26 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 8-24, 26 and 31-33 are pending in this application.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/6/2007 has been entered.

Response to Amendment

3. Applicant's amendment filed 2/6/2007 in response to the previous Office Action (10/30/2006) is acknowledged. The obviousness-type double patenting rejection of claim 8 (items 3-4) and the written description rejection of claims 9-15, 17-24, 26 and 31 under 35 U.S.C. § 112, first paragraph (item 5) have been obviated. The enablement rejection of claims 9-16 (item 6) has been maintained. Note that applicant's amendment also raises new issue that needs further rejection.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-15, 17-23 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In claims 9 and 17, the new proviso "wherein when Ar is a 9-membered bicyclic heterocycle containing one or more heteroatoms selected from N, O and S, Ar is unsubstituted" is a new matter. The concept of linking the substitution of Ar to the definition of Ar = 9-membered bicyclic heterocycle containing one or more heteroatoms selected from N, O and S, is a new concept.

Applicants indicate there is support in the specification at page 4 for said proviso, but there is no written description for the proviso "wherein when Ar is a 9-membered bicyclic heterocycle containing one or more heteroatoms selected from N, O and S, Ar is unsubstituted".

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-16 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is recited a method of inhibiting GSK-3β or the phosphorylation of the Tau protein *in vivo*, but the specification is not enabled for such a scope.

A number of factors are relevant to whether undue experimentation would be required to practice the claimed invention, including "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

(1). Breadth of Claims:

(A) - The scope of use that applicants intend to claim is very broad. According to page 29 of the specification paragraph [0150], "compounds according to the present invention can be used for the inhibition of the kinase GSK-3β. This effect is particularly relevant for the treatment of metabolic diseases such as type I diabetes or neurodegenerative diseases such as Alzheimer's diseases". At page 29 paragraph [0152], it is disclosed examples of diseases which can be treated with the compounds according to the present invention that include strokes, neurodegenerative diseases and cancer. Note that applicants are claiming the treatment of any disease including strokes, neurodegenerative diseases and cancer that require the inhibition of GSK-3β or

the phosphorylation of the Tau protein that is very broad. See previous Office Action for details.

The instant claims 9, 16 and 32 appear to be reach through claim. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all disease, disorders or conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one skill in the art to practice the invention. Note that a method of inhibiting GSK-3β *in vivo* is not different from the claim language "A method of inhibiting GSK-3β in a patient". The claim covers the treatment of any disease that involves inhibition of GSK-3β. This could cover any person healthy or sick.

(B). Scope of Compounds - The scope of the compounds is broad. It is apparent that hundreds of millions of combinations of compounds can be created from the definitions, owing especially to broad scope of A1, A2, and Ar.

(2). Direction of Guidance: The amount of direction or guidance is minimal. The dosage range is 300 fold and hence largely useless. The dosage is completely generic, it is the same regardless of which disorder is being treated.

(3). State of Prior Art: There is no evidence of record that compounds structurally similar to these pyridazine derivative compounds are in use for the treatment of myriad diseases e.g. metabolic disorder, cancer, stroke, neurodegenerative disorders, etc.

(4). Working Examples: There is no any working example that indicates the inhibition of GSK-3β, which in return is presumed to treat myriad diseases e.g. neurodegenerative diseases, strokes, metabolic diseases, syndrome X or immunodeficiency.

(5). Nature of the Invention and Predictability: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(6). The Relative Skill of Those in the Art: The skill level in this art is too low, because no compound effective against e.g. neurodegenerative diseases, strokes, metabolic diseases, syndrome X or immunodeficiency has ever been found.
See previous Office Action for details.

(7). The Quantity of Experimentation Necessary: Immense, especially in view of points (1) and (6).

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Response to arguments

Applicant's argument filed 2/6/2007 has been fully considered but it is not persuasive.

Applicant's argument is carefully reviewed, but it is not sufficient enough to overcome the enablement rejection. Applicants argue, "[d]iscussion of the Wands factors, appears directed to the rejection of original claims 17-28, which recite methods of treating disease, such as neurodegenerative disease and cancer. Thos assertions, however, do not establish the nonenablement of claims 9-16". The examiner disagrees with applicants. Applicants are claiming the inhibition of GSK-3β or the phosphorylation of the Tau protein *in vivo*, which in turn is linked to the treatment of diseases such as cancer, stroke and Alzheimer's disease. According to page 29 of the specification paragraph [0150], "compounds according to the present invention can be used for the inhibition of the kinase GSK-3β. This effect is particularly relevant for the treatment of metabolic diseases ....neurodegenerative diseases such as Alzheimer's diseases". At

page 29 paragraph [0152], it is disclosed examples of diseases, which can be treated with the compounds according to the present invention that include strokes, neurodegenerative diseases and cancer.

Note that claims 9-16 and 32 appear to be reach through claim. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all disease, disorders or conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one skill in the art to practice the invention.

It is recommended that applicants delete claims 9-16 and 32 that are reach through claims. Note that the method of use claims 17-23 are acceptable in terms of the claim language.

Allowable Subject Matter

6. Claims 8, 24, 31 and 33 are allowed.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte whose telephone number is (571) 272-0667. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at (571) 272-0661. The fax phone

number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kahsay Habte
Primary Examiner
Art Unit 1624

February 23, 2007